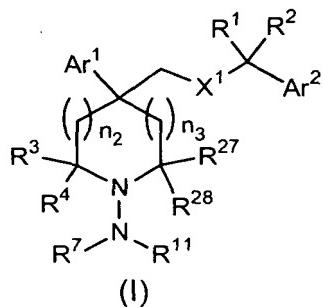


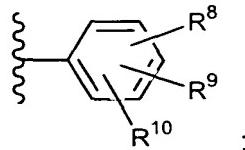
5. What is claimed is:

1. A compound having the formula (I):



or a pharmaceutically acceptable salt or solvate thereof, wherein

10 Ar¹ and Ar² are each independently selected from the group consisting of (R¹⁹)_{n₇}-heteroaryl- and



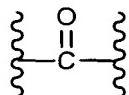
X¹ is selected from the group consisting of -O-, -S-, -SO-, -SO₂-, -NR¹²-, -N(COR¹²)- and -N(SO₂R¹⁵)-;

15 R¹, R³ and R⁵ are each independently selected from the group consisting of H and C₁-C₆ alkyl;

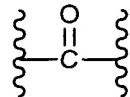
R², R⁴ and R⁶ are each independently selected from the group consisting of H, -CONR¹³R¹⁴ and -(CH₂)_{n₁}-G; wherein G is selected from the group consisting of H, -CF₃, -CHF₂, -CH₂F, -OH, -O-(C₁-C₆)alkyl, -SO₂R¹³, -O-(C₃-C₈ cycloalkyl), -NR¹³R¹⁴, -SO₂NR¹³R¹⁴, -NR¹³SO₂R¹⁵, -NR¹³COR¹², -NR¹²(CONR¹³R¹⁴), -CONR¹³R¹⁴, -COOR¹² and C₃-C₈ cycloalkyl; or

R¹ and R², taken together with the carbon to which they are attached, form a C₃-C₆ cycloalkyl ring; or

R¹ and R², taken together with the carbon to which they are attached, form a

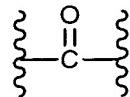


5 group, provided that X1 is -O- or -NR¹² when said



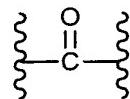
is formed; or

R³ and R⁴, taken together with the carbon to which they are attached, form a



10 group; or

R⁵ and R⁶, taken together with the carbon to which they are attached, form a



group;

R⁷ and R¹¹ are each independently selected from the group consisting of H,

15 C₁-C₆ alkyl, C₃-C₈ cycloalkyl, (R¹⁶)_{n7}-aryl-, (R¹⁹)_{n7}-heteroaryl-, -COOR²⁹, -CONR²¹R²²,
-CON(R²¹)(CH₂)_n-G¹, -S(O)_{n5}(CH₂)_n-G¹, -S(O)_{n5}R¹³, -CO(CH₂)_n-G¹ and -(CH₂)_{n1}-G¹;
wherein

n is 0-4, and

G¹ is selected from the group consisting of H, -OH,

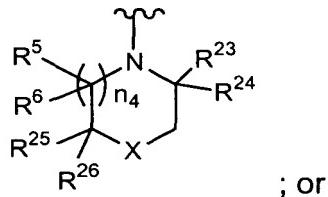
20 (C₁-C₆)alkyl, -O-(C₁-C₆ alkyl), -S(O)_{n5}R¹³, -O-(C₃-C₈ cycloalkyl),
-NR¹³R¹⁴, -SO₂NR¹³R¹⁴, -NR¹³SO₂R¹⁵, -NR¹³COR¹², -NR¹²(CONR¹³R¹⁴),
-OC(=O)R¹², -CONR¹³R¹⁴, -COOR¹², C₃-C₈ cycloalkyl, -CF₃,
(R¹⁶)_{n7}-aryl-O-, (R¹⁶)_{n7}-aryl-, (R¹⁹)_{n7}-heteroaryl-, (R¹⁹)_{n7}-heterocycloalkyl-
and alkenyl, and

25 provided that, when n is 0, then G¹ is selected from the group
consisting of H, (C₁-C₆)alkyl, alkenyl, -CONR¹³R¹⁴, -COOR¹², C₃-C₈
cycloalkyl, -CF₃, (R¹⁶)_{n7}-aryl-, (R¹⁹)_{n7}-heteroaryl-, and
(R¹⁹)_{n7}-heterocycloalkyl-; and

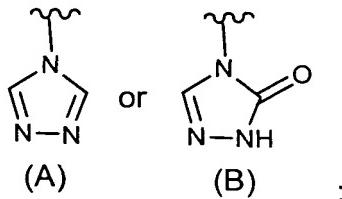
provided that, when n₁ is 1, then G¹ is selected from the group
30 consisting of H, (C₁-C₆)alkyl, alkenyl, -S(O)_{n5}R¹³, -SO₂NR¹³R¹⁴,

5 -CONR¹³R¹⁴, -COOR¹², C₃-C₈ cycloalkyl, -CF₃, (R¹⁶)_{n7}-aryl-,
(R¹⁹)_{n7}-heteroaryl- wherein said heteroaryl ring is bound by a ring carbon
to the -(CH₂)_{n1}- group, and (R¹⁹)_{n7}-heterocycloalkyl- wherein said
heterocycloalkyl ring is bound by a ring carbon to the -(CH₂)_{n1}- group; or
R⁷ and R¹¹, taken together with the nitrogen to which they are attached, form a
10 5-7 membered heterocycloalkyl ring of the following formula:

10 5-7 membered heterocycloalkyl ring of the following formula:



R^7 and R^{11} , taken together with the nitrogen to which they are attached, form a 5-membered ring having the formula (A) or (B):



15 X is selected from the group consisting of $-NR^{20}-$, $-N(CONR^{13}R^{14})-$,
 $-N(CO_2R^{13})-$, $-N(SO_2R^{15})-$, $-N(COR^{12})-$, $-N(SO_2NHR^{13})-$, $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-CF_2-$,
 $-CH_2-$, and $-C(R^{12})F-$;

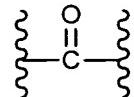
R⁸, R⁹ and R¹⁰ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, -OR¹², halogen, -CN, -NO₂, -CF₃, -CHF₂, -CH₂F, -OCF₃, -OCHF₂, -OCH₂F, -COOR¹², -CONR²¹R²², -NR²¹COR¹², -NR²¹CO₂R¹⁵, -NR²¹CONR²¹R²², -NR²¹SO₂R¹⁵, -NR²¹R²², -SO₂NR²¹R²², -S(O)_{n5}R¹⁵, (R¹⁶)_{n7}-aryl- and (R¹⁹)_{n7}-heteroaryl-;

R^{12} is selected from the group consisting of H, C₁-C₆ alkyl and C₃-C₈ cycloalkyl;

R^{13} and R^{14} are each independently selected from the group consisting of H,

25 C₁-C₆ alkyl, C₂-C₃ alkyl-O-CH₃, C₃-C₈ cycloalkyl, (R¹⁹)_{n7}-aryl(CH₂)_{n6}- and
(R¹⁹)_{n7}-heteroaryl-(CH₂)_{n6}-; or

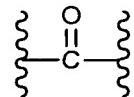
- 5 R^{13} and R^{14} , taken together with the nitrogen to which they are attached, form a
 4-7 membered ring containing from 0-3 additional heteroatoms selected from the
 group consisting of -O-, -S- and $-NR^{12}-$;
- 10 R^{15} is C_1-C_6 alkyl, C_3-C_8 cycloalkyl or $-CF_3$;
 10 R^{16} is 1 to 3 substituents each independently selected from the group
 consisting of C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_1-C_6 alkoxy, halogen and $-CF_3$;
- 15 R^{19} is 1 to 3 substituents each independently selected from the group
 consisting of C_1-C_6 alkyl, C_3-C_8 cycloalkyl, -OH, halogen, -CN, $-NO_2$, $-C(O)CF_3$,
 $-CF_3$, $-CHF_2$, $-CH_2F$, $-OCF_3$, $-OCHF_2$, $-OCH_2F$, $-O-(C_1-C_6$ alkyl), $-O-(C_3-C_8$ cycloalkyl),
 $-COOR^{12}$, $-CONR^{21}R^{22}$, $-NR^{21}R^{22}$, $-NR^{21}COR^{12}$, $-NR^{21}CO_2R^{12}$, $-NR^{21}CONR^{21}R^{22}$,
 15 $-NR^{21}SO_2R^{15}$ and $-S(O)_{n5}R^{15}$;
- 20 R^{20} is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, $-(CH_2)_{n6}$ -heterocycloalkyl,
 $(R^{19})_{n7}$ -aryl($CH_2)_{n6}$ - or $(R^{19})_{n7}$ -heteroaryl- $(CH_2)_{n6}$ -;
- 20 R^{21} and R^{22} are each independently selected from the group consisting of H,
 C_1-C_6 alkyl, C_3-C_8 cycloalkyl and benzyl; or
- 20 R^{21} and R^{22} , taken together with the nitrogen to which they are attached, form a
 4-7 membered heteroaryl ring containing from 0-3 additional heteroatoms selected
 from the group consisting of -O-, -S- and $-NR^{12}-$;
- 25 R^{23} and R^{24} are each independently selected from the group consisting of H,
 C_1-C_6 alkyl and $-CONR^{13}R^{14}$; or
- 25 R^{23} and R^{24} , taken together with the carbon atom to which they are attached,
 form a
-
- group;
- 30 R^{25} , R^{26} , R^{27} and R^{28} are each independently selected from the group
 consisting of H and C_1-C_6 alkyl; or
- 30 R^{25} and R^{26} , taken together with the carbon atom to which they are attached,
 form a



5

group; or

R^{27} and R^{28} , taken together with the carbon atom to which they are attached, form a



10 group;

R^{29} is selected from the group consisting of C₁-C₆ alkyl and C₃-C₈ cycloalkyl;

n_1 is 1-4;

n_2 and n_3 are each independently 0-3, provided that a sum of n_2 and n_3 is 0-4;

n_4 is 0-2;

15 n_5 is 0-2;

n_6 is 0-3; and

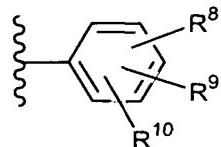
n_7 is 0-3; and

provided that, when n_4 is 0, and R^{25} and R^{26} are each H, then X is not -O-, -NR²⁰- or -S-.

20

2. The compound of Claim 1 wherein X¹ is -O-.

3. The compound of Claim 1 wherein Ar¹ and Ar² are each independently



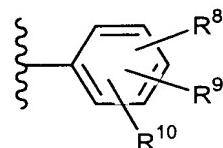
25

4. The compound of Claim 3 wherein R⁸, R⁹ and R¹⁰ are each independently selected from the group consisting of H, -CH₃, halogen and -CF₃.

5. The compound of Claim 1 wherein

X^1 is -O-; and

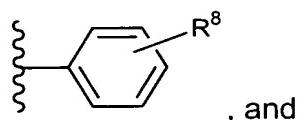
Ar^1 and Ar^2 are each independently



wherein R^8 , R^9 and R^{10} are each independently selected from the group consisting of
10 H, -CH₃, halogen and -CF₃.

6. The compound of Claim 1 wherein

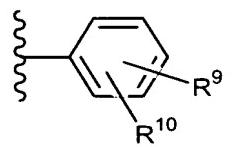
Ar^1 is



, and

15

Ar^2 is



wherein,

R^8 is selected from the group consisting of H and F, and

20 R^9 and R^{10} are each independently selected from the group consisting of
H, -CH₃, F, Cl and -CF₃.

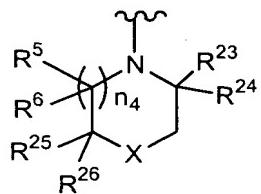
7. The compound of Claim 6 wherein

X^1 is -O-; and

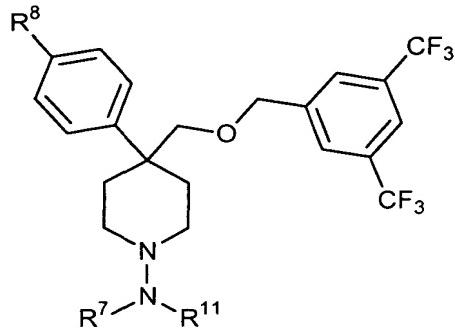
25 R^3 , R^4 , R^{27} and R^{28} are each H.

8. The compound of Claim 6 wherein R^5 and R^6 are H.

5 9. The compound of Claim 7 wherein R⁷ and R¹¹, taken together with the nitrogen to which they are attached, form a 5-7 membered ring having the following formula:



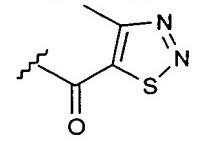
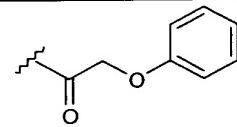
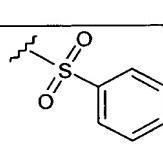
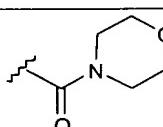
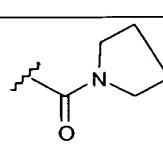
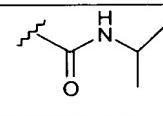
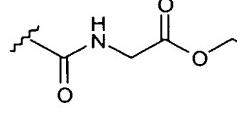
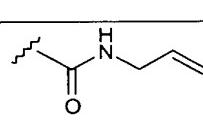
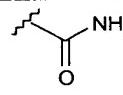
10 10. The compound of Claim 1 having the formula



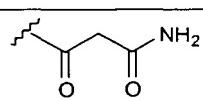
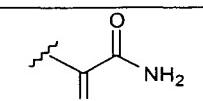
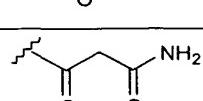
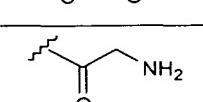
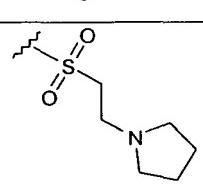
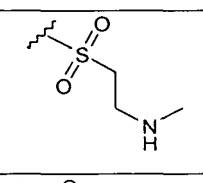
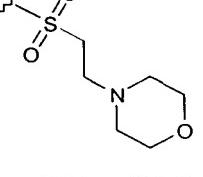
wherein R⁷, R⁸ and R¹¹ are selected from the group consisting of:

R ⁸	R ⁷	R ¹¹
H	H	H
H	H	
H	H	
H	H	
H	H	

H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	

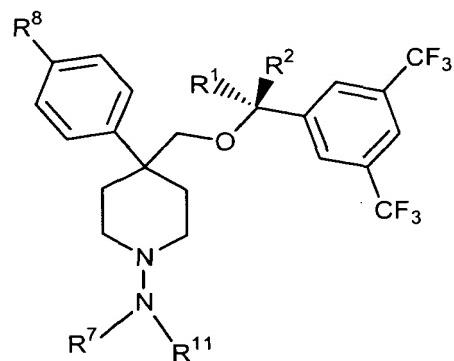
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	

H		
H		
F	H	
F	H	H
F	H	
F	H	
F	H	
F	H	
F	H	
F	H	
H	H	

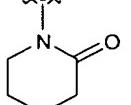
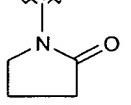
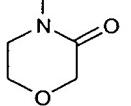
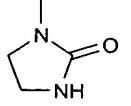
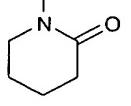
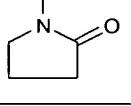
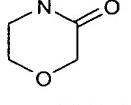
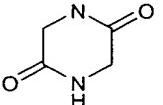
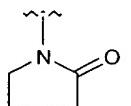
H	H	
F	H	
F	H	
H	H	
H	H	
H	H	
H	H	

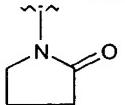
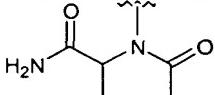
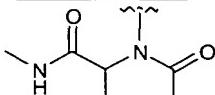
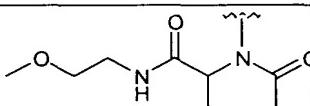
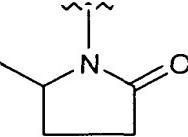
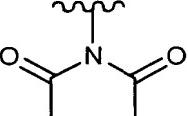
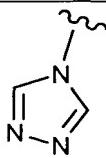
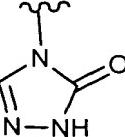
5

11. The compound of Claim 1 having the formula:

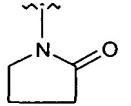
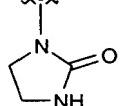
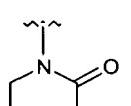
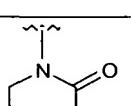
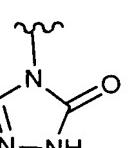


wherein R¹, R², R⁷, R⁸ and R¹¹ are selected from the group consisting of:

R^8	R^1	R^2	$-NR^7R^{11}$
H	H	H	
H	H	H	
H	H	H	
H	H	H	
F	H	H	
F	H	H	
F	H	H	
H	H	H	
H	H	CH ₃	

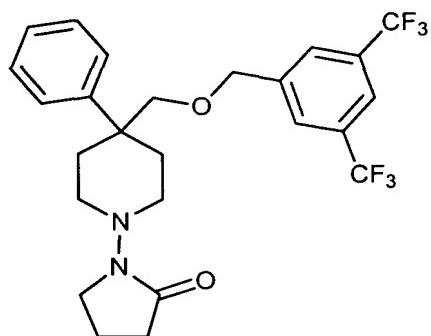
H	H	CH ₂ OH	
H	H	H	
H	H	H	
H	H	H	
H	H	H	
H	H	H	
H	H	H	
H	H	H	

12. The compound of Claim 11 or the pharmaceutically acceptable salt or solvate thereof, wherein R¹, R², R⁷ R⁸ and R¹¹ are selected from the group consisting of

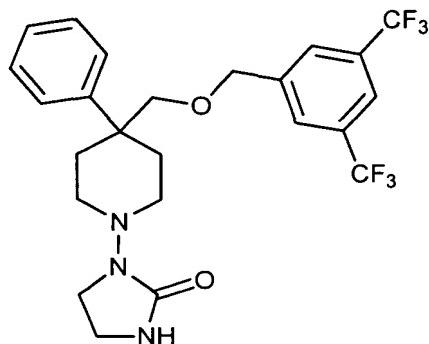
R^8	R^1	R^2	$-NR^7R^{11}$
H	H	H	
H	H	H	
H	H	CH ₃	
H	H	CH ₂ OH	
H	H	H	

5

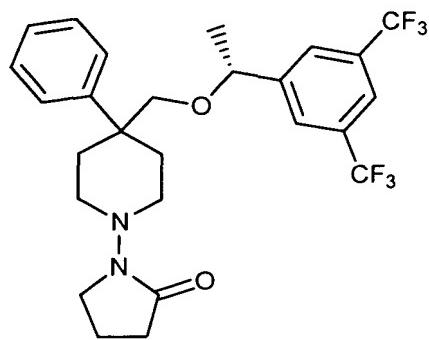
13. The compound of Claim 12 having the formula:



5 14. The compound of Claim 12 having the formula:

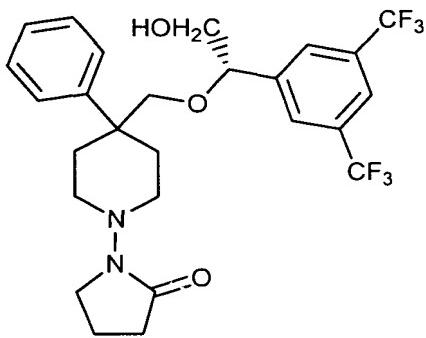


15. The compound of Claim 12 having the formula:

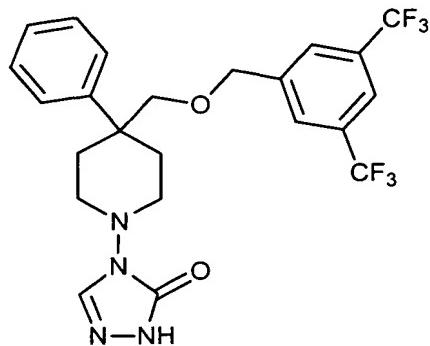


10

16. The compound of Claim 12 having the formula:



5 17. The compound of Claim 12 having the formula:



18. A pharmaceutical composition comprising at least one compound of Claim 1, and a pharmaceutically acceptable carrier.

10

19. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, at least one serotonin reuptake inhibitor, and at least one compound of Claim 1.

15

20. A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1, wherein said physiological disorder, symptom or disease is selected from the group consisting of: respiratory diseases, inflammatory diseases, skin disorders, ophthalmological disorders, central nervous system conditions, addictions, epilepsy, nociception, psychosis, schizophrenia, Alzheimer's disease, AIDS related dementia, Towne's disease, stress related disorders, obsessive/compulsive disorders, eating disorders, sleep disorders, mania, premenstrual syndrome, gastrointestinal disorders, atherosclerosis, fibrosing disorders, obesity, Type II diabetes, pain related disorders, bladder and genitourinary disorders, and nausea.

25

21. A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective

5 amount of at least one compound of Claim 1, wherein said physiological disorder,
symptom or disease is selected from the group consisting of: a respiratory disease,
depression, anxiety, phobia, bipolar disorder, alcohol dependence, psychoactive
substance abuse, nociception, psychosis, schizophrenia, stress related disorder,
obsessive/compulsive disorder, bulimia, anorexia nervosa, binge eating, sleep
10 disorder, mania, premenstrual syndrome, gastrointestinal disorder, obesity, headache,
neuropathic pain, post-operative pain, chronic pain syndrome, bladder disorder,
genitourinary disorder, cough, emesis and nausea.

22. A method for treating a physiological disorder, symptom or disease in a
15 patient in need of such treatment, comprising administering to said patient an effective
amount of at least one compound of Claim 1, and an effective amount of at least one
active ingredient selected from the group consisting of: other NK₁ receptor
antagonists, selective serotonin reuptake inhibitors, dopamine receptor agonists,
serotonin 5-HT₃ receptor antagonists, serotonin 5-HT_{2c} receptor agonists, nociceptin
20 receptor agonists, glucocorticoids and inhibitors of multidrug resistance protein 5,
wherein said physiological disorder, symptom or disease is selected from the group
consisting of: a respiratory disease, depression, anxiety, phobia, bipolar disorder,
alcohol dependence, psychoactive substance abuse, nociception, psychosis,
schizophrenia, stress related disorder, obsessive/compulsive disorder, bulimia,
25 anorexia nervosa, binge eating, sleep disorder, mania, premenstrual syndrome,
gastrointestinal disorder, obesity, headache, neuropathic pain, post-operative pain,
chronic pain syndrome, bladder disorder, genitourinary disorder, cough, emesis and
nausea.

30 23. A method of treating emesis and/or nausea in a patient in need of such
treatment comprising administering to said patient an effective amount of at least one
compound having the formula (I) in combination with an effective amount of at least
one serotonin 5-HT₃ receptor antagonist and/or at least one glucocorticoid.

5 24. The method of Claim 23 wherein said serotonin 5-HT₃ receptor antagonist is ondansetron and said glucocorticoid is dexamethasone.

10 25. The method of Claim 21, wherein the physiological disorder, symptom or disease is emesis, depression, anxiety or cough.

15 26. The method of Claim 25 wherein the physiological disorder, symptom or disease is depression or anxiety.

20 27. The method of Claim 26, further comprising administering to the patient an effective amount of at least one anti-depressant agent and/or at least one anti-anxiety agent.

25 28. The method of Claim 25 wherein depression is being treated and said method further comprises administering to the patient an effective amount of at least one selective serotonin reuptake inhibitor.

25 29. A method for antagonizing an effect of a Substance P at a neurokinin-1 receptor site or for blocking at least one neurokinin-1 receptor, in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1.

30 30. A kit comprising, in separate containers in a single package, pharmaceutical compositions for use in combination to treat an NK₁ receptor mediated disease, wherein one container comprises a pharmaceutical composition comprising an effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier, and wherein, a separate container comprises a pharmaceutical composition comprising another therapeutic agent in a pharmaceutically acceptable carrier, said therapeutic agent being selected from the group consisting of: SSRIs, other types of NK₁ receptor antagonists, prostaglandins, H₁ receptor antagonists, α-

- 5 adrenergic receptor agonists, dopamine receptor agonists, melanocortin receptor
agonists, endothelin receptor antagonists, endothelin converting enzyme inhibitors,
angiotensin II receptor antagonists, angiotensin converting enzyme inhibitors, neutral
metalloendopeptidase inhibitors, ET_A antagonists, renin inhibitors, serotonin 5-HT₃
receptor antagonists, serotonin 5-HT_{2c} receptor agonists, nociceptin receptor
10 agonists, glucocorticoids, rho kinase inhibitors, potassium channel modulators and
inhibitors of multi-drug resistance protein 5.

31. A kit comprising, in separate containers in a single package,
pharmaceutical compositions for use in combination to treat depression and/or
15 anxiety, wherein one container comprises a pharmaceutical composition comprising
an effective amount of a compound of Claim 1 in a pharmaceutically acceptable
carrier, and wherein, a separate container comprises a pharmaceutical composition
comprising an antidepressant agent in a pharmaceutically acceptable carrier, and/or
wherein a separate container comprises a pharmaceutical composition comprising an
20 antianxiety agent in a pharmaceutically acceptable carrier.

32. A kit comprising, in separate containers in a single package,
pharmaceutical compositions for use in combination to treat an NK₁ receptor
mediated disease, wherein one container comprises a pharmaceutical composition
25 comprising an effective amount of a compound of Claim 1 in a pharmaceutically
acceptable carrier, and wherein, a separate container comprises a pharmaceutical
composition comprising an SSRI in a pharmaceutically acceptable carrier.

33. A kit comprising, in separate containers in a single package,
30 pharmaceutical compositions for use in combination to treat depression and/or
anxiety, wherein one container comprises a pharmaceutical composition comprising
an effective amount of a compound of Claim 1 in a pharmaceutically acceptable
carrier, and wherein, a separate container comprises a pharmaceutical composition
comprising an SSRI in a pharmaceutically acceptable carrier.

5

34. A kit comprising, in separate containers in a single package, pharmaceutical compositions for use in combination to treat emesis and/or nausea, wherein one container comprises a pharmaceutical composition comprising an effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier, and wherein, a separate container comprises a pharmaceutical composition comprising a serotonin 5-HT₃ receptor antagonist in a pharmaceutically acceptable carrier, and/or wherein a separate container comprises a pharmaceutical composition comprising a glucocorticoid in a pharmaceutically acceptable carrier.
- 10
35. A kit comprising, in separate containers in a single package, pharmaceutical compositions for use in combination to treat emesis and/or nausea, wherein one container comprises a pharmaceutical composition comprising an effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier, and wherein, a separate container comprises ondansetron, and/or wherein a separate
- 15
- 20 container comprises dexamethasone.